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THE PHENOTYPE OF ASTHMA AND ALLERGIC RHINITIS

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Allergy in the twenty-first century. has become a global problem with significant medical, social and economic losses worldwide. Its prevalence increases with each passing year and becomes signs of a pandemic. Thus, according to the World Organization for Allergy (WAO - 2013p.), 150 million Europeans suffer from allergic diseases, and by the beginning of 2025 half of the population in Europe will have one or another allergic disease [1].

Allergic respiratory diseases, asthma and rhinitis, are rightly called the 21st century epidemic and modern age diseases. Although modern medicine offers a variety of preventive and therapeutic strategies, the prevalence of these diseases has been dramatically increasing in both developed and undeveloped countries across the world, especially in children and young adult. The WAO estimates there are 300 million asthmatics in the world, and 500 million people with the symptoms of rhinitis [1]. Very often, asthma and rhinitis coexist in one patient. Numerous contemporary studies, guided by the concept “one airway – one disease”, have revealed the epidemiological, pathophysiological and clinical correlation of asthma and allergic rhinitis (AR) [2].

The most common chronic allergic diseases in the world today are asthma and allergic rhinitis (AR). According to epidemiological statistics, 44-68% of patients in AR have asthma, and in 76 - 80% of patients with asthma have comorbid AR [2]. There is also a chronological relationship between AR and asthma, which has been repeatedly confirmed by research. Data from the BAMSE cohort (Sweden, 2012) showed that in children aged 1 year, asthma is associated with rhinitis and / or atopic

dermatitis (AD) in 38% of cases, and to 12 years of age, this figure increases to 67% [3]. AR is very often an initial manifestation of systemic allergy in the respiratory tract, and eventually the full allergic cascade starts to reach the lower respiratory tract "in the variant of the allergic march" [2, 3]. Other authors note that in children of early age, AR is often not diagnosed due to frequent respiratory infections [4]. Asthma and AR as nosologies have always been considered in detail: diagnosed and treated in different ways, but recent studies have suggested that upper and lower respiratory tract on upper respiratory tract (URT) and lower respiratory tract (LRT) are a manifestation of a single inflammatory process (the hypothesis of "the only respiratory disease" (united airway disease hypothesis)) [5, 6]. The relationship between AR and asthma has been repeatedly found in scientific publications [7, 8], which confirmed the affinity of the anatomy of the mucous membrane of URT and LRT and the course of pathophysiological processes in them. Inflammation of AR and asthma occurs with the participation of identical triggers, immunocompetent cells, inflammatory mediators. Allergic respiratory syndrome - the phenomenon of allergic rhinitis and reverse broncho-obstruction is considered as a manifestation of the same disease in URT and LRT [9]. There are several mechanisms by which allergic inflammation spreads to LRT: allergic mediators from the nose penetrate the LRT with blood flow or by direct drainage, which leads to inflammation and hyperreactivity of the bronchi; through nasal sinus-bronchial reflexes - that is, stimulation of the receptors of the nose and the sinuses leads to reflex bronchospasm. During the symptoms of AR, the inflow of allergens, cold and dry air through the mouth also increases, which also contributes to bronchospasm [10]. In 15-65%, and according to some data [11], 80% of patients with AR have a typical functional marker of asthma - hyperreactivity of the respiratory tract (HRT), where the severity of the course of nasal symptoms is closely correlated with the bronchial caliber and the degree of HRT. In clinical practice, there are frequent cases in which patients with isolated AR show a deterioration in spirometry and/or HRT [12]. It is proved that asthma with AR is characterized by a more pronounced lability of the bronchi due to the bronchodilation reaction to the short-acting β 2-adrenomimetic agent.

In some studies, the association between the presence of AR and the severity of asthma has been proved [13]. Patients with asthma with concomitant AR often needed unscheduled hospitalizations and higher economic costs for treatment. According to some studies, patients with asthma with comorbid AR had a significantly more inflammatory process than patients without AR. Thus, the level of nitric oxide and eosinophils in blood was 2 times higher, and the level of total serum IgE was significantly higher than in patients without AR [14].

Long-term observational studies have shown that AR often precedes asthma. Thus, according to data from 23 years of observation, patients with AR of asthma developed 3 times more often than in patients without AR, and the ratio of chances of association of AR-asthma after 7 years of observation was 7.1 versus 3.9 in control [11]

In most patients with asthma with concomitant AR (65.7%), the course of asthma is uncontrollable. Significant frequency of cases (81.0%) of subjective underestimation by patients in their state compared with the results of the ACT test [15, 16]

One of the most important aspects of inadequate asthma control is its phenotypic heterogeneity. Clinical phenotypes of asthma are heterogeneous. Their formation depends on genetic and environmental influences and is determined by the interaction of the cellular elements of the respiratory tract and the immune system [17]. Phenotyping takes place in two directions: clinical, pathophysiological, molecular markers [17, 18] and options for response to therapy [17]. This explains a large number of genotypes and phenotypes of asthma. The genotype of asthma is determined by the type of inflammation: eosinophilic, neutrophilic, mixed, non-granulocytic.

THE AIM

The purpose of the work was to analyze the features of the genotype and phenotype in patients with a co-morbidity of bronchial asthma and allergic rhinitis.

MATERIALS AND METHODS

A total of 115 patients with asthma were examined on the basis of the SDC "Rehabilitation" of the Ministry of Health of Ukraine in Uzhhorod. All patients had a thorough allergy history, anamnesis of life and disease. Conducted general clinical and diagnostic examination. The function of external respiration (FER) was investigated using the computer spirograph "Pulmovent-2". To determine the features of the co-morbid flow of asthma from AR, all patients were divided into two groups. To the first (I) group included 58 patients with allergic asthma from AR, to the second (II) - 57 patients with asthma (non-allergic) without AR.

RESULTS

The average age in the group of patients with asthma in AR was 29.2 ± 0.68 years, and in the group of patients with isolated asthma was significantly higher and amounted to 38.2 ± 0.76 years. By gender, both groups were dominated by women. The duration of asthma in both groups was almost the same and was 11.1 ± 1.87 years in the first group and 11.6 ± 1.96 years in the second group. While the age of the debut of asthma varied. Thus, in the first group of patients, the age at which debuted asthma was 18.0 ± 1.43 years versus 26.6 ± 1.66 years - in the second group. Formation of asthma in patients with AR was characterized by the onset of symptoms of AR in $(2,5 \pm 0,55)$ years. These data are consistent with the literature data that asthma with AR is formed "in the alternative of an allergic march," when the onset of the allergic process was AD and / or AR [19].

All patients had a thorough allergy history. In the I group of patients, a high indicator of sensitization to household and pollen allergens was established in 50 (86.2%) patients. In the II group, the indicator was significantly lower and amounted to 36 (63.2%) cases, mainly to household chemicals, sharp odors, food allergens.

With the study of hereditary history in patients with asthma with AR, a variety of manifestations of allergy in the family were detected in 38 (65.5%) cases. Among these patients, the presence of allergic diseases in relatives of the I-II line of mother affinity was detected in 22 (57.9%) patients, from the father - in 15 (39.4%) patients

and from both parents in 1 (2.7%) of the patient. In the group of patients with atopic asthma heredity was diagnosed in 24 (42.1%) patients, mainly on the maternal line.

In the I group of patients, AR was more often combined with intermittent and persistent asthma of the lung in 42 (72.4%) cases. In addition, in this group of patients also were diagnosed: in 12 (20.7%) cases of professional asthma and 3 (5.2%) - aspirin asthma. The second group consisted mainly of patients with persistent asthma of the mild and moderate course.

Medicinal allergy in the group of patients with asthma with AR was reported in 14 (24.1%) cases to analgin, aspirin, anesthetics. In the comparison group, drug allergy was detected in 19 (33.3%) cases of euphylline, the antibiotics of the penicillin number.

AR in the I group of patients was divided into seasonal allergic rhinitis (SAR) in 48 (82.8%) cases and year-round allergic rhinitis (YRAR) in 10 (17.2%) cases. The YRAR was characterized by the presence of persistent symptoms. The main reasons were domestic dust, household dust mites, mold allergens, cockroaches and others. The cause of SAR was the seasonal appearance of allergenic particles in the air (pollen of plants, trees). It was sometimes difficult to diagnose SAR or YRAR. Thus, in patients with SAR as a result of the trigger action of several seasonal allergens, symptoms were manifested year-round. In turn, the YRAR was sometimes additionally accompanied by the effects of several seasonal allergens. Regardless of the type of AR, the clinical symptoms of the disease were not discrepancies. AR was manifested by symptoms such as difficult nasal breathing, abundant watery discharge from the nasal cavity (rhinorrhea), itching in the nasal cavity, swollen sneezing.

Clinical symptoms of AR were ranked according to the intensity of manifestations (0 absent, lung-1, average gravity-2, severe-3), with the total number of points deducted in accordance with the International Total Score System – Total Symptoms Score (TSS), as well as using the visual analog scale (VAS). TSS in the group of patients with asthma with AR was 8.75 ± 2.01 and VAS – 6.50 ± 1.05 points.

In the comparison group, non-allergic (vasomotor) rhinitis (NAR) was determined in 11 (19.3%) patients. The NAR clinic was distinct from AR, first of all, in the absence of pruritus in the nasal cavity and an attack-like sneezing. NAR increased when the body position changed.

Among the causes of the first attack of myocardial infarction in the I group of patients dominated contact with pollen and everyday allergens in 52 (89.7%) cases. In the II group of patients, the reasons for the formation of non-allergic asthma were called complications after transmitted pneumonia in 35 (61,4%) patients.

The incidence of asthma in the group of patients with AR was 3.2 ± 0.78 times a year, whereas in the comparison group only 1.8 ± 0.54 times a year. Season of exacerbation of asthma in two groups varied. In group I, 48 (82.8%) patients had asthma exacerbations in the spring and / or autumn, whereas in group II in 50 (87.7%) patients - for the winter and autumn.

All patients were examined for the function of external respiration (FER). The lung of the forced vital capacity of the lungs (FVC) was lowered in the I group of patients in 32 (52,2%) cases, and in the II group - in 38 (66,7%) cases. The obstruction of distal bronchus in the group of patients with asthma with AR was 24 (41.4%) cases and correlated with symptoms of difficult nasal breathing. For the II group of patients, generalized obstruction of the bronchi was characteristic in 27 (47.4%) cases.

The bronchial lability was determined according to the recommendations [20] by assessing their response to metered physical activity and inhalation of short-acting β_2 -adrenomimetic agents (200 μg of salbutamol), followed by the calculation of bronchial lability as a sum of components - the bronchoconstriction index (IBC) and bronchodilation (IBD) Positive considered a sample of salbutamol with an index of IBD more than 12%. The index of bronchospasm in the group of patients with asthma with AR was $11,7 \pm 1,82\%$, and in the group of patients with atopic asthma - $10,9 \pm 2,01\%$. The dilatation index in the I group of patients was $12.6 \pm 2.11\%$, whereas in the II group - $6.8 \pm 1.90\%$. Thus, the lability index in the first group was $24.3 \pm 2.74\%$ against - $17.7 \pm 3.22\%$ in the second group of patients.

Inflammation of the respiratory tract was determined by general clinical, biochemical and immunological methods. Thus, the titre of total serum IgE in the group of patients with allergic asthma with AR was 19.5 ± 1.31 IU against 8.6 ± 1.13 IU in the comparison group. The level of eosinophils in the peripheral blood was also an order of magnitude higher in Group I compared with the II group of patients and was $9.8 \pm 0.62\%$ and $3.8 \pm 0.44\%$ respectively. Histamine of blood serum in the group of patients with allergic asthma with AR was significantly higher than that in the group of patients with non-allergic asthma and was 2.12 ± 0.05 mlmol / l and 1.44 ± 0.05 mlmol / l, respectively ($p < 0.001$). Histamine excretion was decreased and in the I group it was $13.1 \pm 0.93\%$, whereas in the II group it was at $19.0 \pm 1.19\%$. Cholinesterase activity was decreased in the I group to 20.7 ± 1.94 and in the second group to 13.9 ± 1.43 ($p < 0.05$). Various violations and type of inflammation in the respiratory system correlated with changes in the NO - producing system. Thus, the level of NO₂ in the condensate of exhaled air was 9.64 ± 0.31 mlmol / l in the I group, whereas in the second group it was only 3.20 ± 0.14 mlmol / l ($p < 0.05$).

The level of control of symptoms of asthma was determined by the Asthma Control (ACT) test. Patients were asked to answer 5 questions about asthma during the last 4 weeks. The score from 5 to 25 corresponded to different degrees of asthma control. So, the sum of points up to 20 - indicated the uncontrollability of the course of the disease. In the I group, uncontrolled asthma was in 38 (65.5%) patients, whereas in the second group only 19 (33.3%). In addition, in patients with allergic asthma with AR, more pronounced nocturnal asthma symptoms 43 (74.1%) versus 22 (38.6%) in the non-allergic asthma group were more pronounced. The number of use of β_2 - adrenomimetics per day in group I was significantly higher - 286 inhalations versus 154 in group II, apparently due to symptoms of AR, which worsened the patient's condition, especially at night.

DISCUSSION

Thus, after the conducted studies it can be stated that the comorbidity of allergic asthma with AR has its own peculiarities and this group of patients can be considered as a separate phenotype of asthma [17]. This group of patients is characterized by the

first manifestation of allergy in childhood. This, as a rule, is AR and / or AD, which is consistent with the data of literature [2, 3, 4]. For this cohort of patients also characterized by a burdened family allergic anamnesis [21]. The debut of allergic asthma in these patients begins at adolescence or adolescence against the background of diagnosed AR (pollen allergy), AD "in the variant of an allergic march [4, 19]. Such patients often show sensitization to household and pollen allergens, drug allergy to non-steroidal anti-inflammatory drugs and anesthetics. Among the causes of allergic asthma, contact with household and pollen allergens is prevalent. Characteristic high frequency of exacerbations with seasonality - spring and / or autumn. The comorbidity of the two diseases also requires higher economic costs [13, 21]. Symptoms of AR and asthma interact with one another. And as a result - more often the use of medicines. Also, the correlation of AR symptoms with obstructive distal bronchus is characteristic, the lability of the bronchi is expressed.

Patients with allergic asthma with AR have a more pronounced IgE-dependent type of inflammatory process. Thus, the level of total serum IgE and blood eosinophils has increased by more than 2 times, which is in agreement with the data of other scientists [5, 8, 22], that the clinical symptoms of AR and asthma (nasal congestion and bronchospasm) are caused by IgE - dependent inflammation in response to the action of allergens. For this cohort is also characterized by high levels of histamine, reduced histamine secretion and cholinesterase activity of almost 1.5 times. The level of NO₂ in the condensation of exhaled air in patients with allergic asthma with AR is significantly higher than in patients with non-allergic asthma (2-3 times), which is confirmed by data from other studies [8, 14] and is explained by a significant level of allergy to the organism and manifestation of clinical symptoms of AR .

The presence of patients with allergic asthma in the associated AR affects the severity of asthma and the level of control. Asthma control is significantly worse (2 times) due to nightly, daytime symptoms of AR, which in turn increases the use of fast drugs in 1.9 times [13, 15, 23, 24].

CONCLUSION

All of the above suggests that patients with bronchial asthma with concomitant allergic rhinitis form a separate phenotype of asthma. Understanding the features of the course of asthma where allergic rhinitis initiates and complicates its course, taking into account the features of pathogenesis and functional unity of the respiratory tract allows us to work out the strategy of combined therapy of both diseases, aimed at optimizing the effectiveness, safety and cost savings for the treatment of this group of patients.

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АПЛІКАЦІЯ ЯК ЗАСІБ РОЗВИТКУ ТВОРЧИХ ЗДІБНОСТЕЙ ДІТЕЙ ДОШКІЛЬНОГО ВІКУ

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В історії дошкільної педагогіки проблема творчості є однією з найактуальніших. У всі часи потрібні були творчі особистості, оскільки нестандартні рішення є двигунами науки, техніки, культури. І саме творчі люди, а не виконавці, створюють все нове, визначальне, прогресивне.

Наш час вимагає творчих, нестандартних, мислячих і діючих людей на благо розвитку особистості і суспільства.

Тому соціальне замовлення суспільства - розвиток і виховання творчості у дітей, що вирішує нагальне завдання формування творчого потенціалу всього суспільства, забезпечує можливість інтенсивного соціального та науково-технічного прогресу, розвитку науки і культури, виробництва і соціального життя.

Формування творчої особистості - одне з важливих завдань педагогічної теорії і практики на сучасному етапі, вирішення якого має розпочатися вже в дошкільному дитинстві, тому дошкільний вік сенситивний, найбільш сприятливий для розвитку не тільки образного мислення, а й уяви, психічних процесів, що становить основу творчої діяльності.